PTO/SB/17 (01-03)
Approved for use through 04/30/2003. OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 210

Complete if Known	
Application Number	09/825,246
Filing Date	April 2, 2001
First Named Inventor	Singh
Examiner Name	J. Tung
Group / Art Unit	1637
Attorney Docket No.	033.05US

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 50-2266

Deposit Account Name: Aclara Biosciences, Inc.

The Commissioner is authorized to: *(check all that apply)*
☒ Charge fee(s) indicated below ☒ Credit any overpayments
☒ Charge any additional fee(s) during the pendency of this application
☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. EXTRA CLAIM FEES

			Extra Claims		Fee from below		Fee Paid
Total Claims		-20 ** =	0	X		=	0
Independent Claims		-3 ** =	0	X		=	0
Multiple Dependent				X		=	0

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	210
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,300	2453	650	Petition to revive – unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17 (q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) ____

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($) 210

SUBMITTED BY					Complete *(if applicable)*
Name (Print/Type)	Stephen C. Macevicz	*Registration No. Attorney/Agent)*	30,285	*Telephone*	(650) 210-1223
Signature				*Date*	10 June 2004

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

OFFICIAL

CERTIFICATION OF FACSIMILE TRANSMISSION
I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below:

Virginia Griffith — 10 June 2004 (Date) — Pages transmitted (incl cover): 6

Destination FAX number: (703) 872-9306

Case No. **033.05** (0225-0033.20)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s):	Sharat Singh et al		
Serial No:	09/825,246	Examiner:	**J. Tung**
Filed:	02 April 2001	Art Unit:	**1637**
For:	SETS OF OLIGONUCLEOTIDE-BINDING E-TAG PROBES	Confirmation No.	**4459**

RESPONSE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action dated 20 January 2004, Applicants submit the following remarks.

REMARKS

No claim has been amended or cancelled. Claims 16-17 and 19-29 are currently pending in the application.

Rejections Under 35 U.S.C. 103

In paragraph 5 of the Office Action, the Examiner rejected claims 16-17, 19-21, and 23-28 under 35 U.S.C. 103(a) as being unpatentable over Grossman (U.S. patent 5,470,705) in view of Kline (U.S. patent 5,459,078). The Examiner appears to argue as follows: Grossman describes a

technique for detecting a plurality of target polynucleotides that includes binding polymers with fluorescently labeled polymeric tails that have, or impart to the binding polymers, distinctive electrophoretic mobilities for separation and detection; thus, Grossman discloses the elements of Applicants' electrophoretic probes, except for capture ligands. Kline discloses an assay system employing a capture reagent comprising analyte-specific binding compounds attached to an anionic polymer. After analyte binds to the binding compounds (either displacing labeled analyte in the competitive format or further binding with a labeled antibody in the sandwich format), the entire complex is captured by an oppositely charged (cationic) solid phase. One of ordinary skill in the art would be motivated to add a biotin (or like capture ligand) to Applicants' electrophoretic probes in order to use an ion-capture reagent of Kline employing avidin (or like binding compound) to impart a charge to the probes opposite to that of the released eTag reporters of Applicants' invention.

Applicants respectfully disagree. Kline at most discloses an immunoassay employing a soluble capture reagent comprising multiple binding compounds, such as analyte-specific antibodies, bound to an anionic polymer. After incubation with a sample that contains analyte (and perhaps, in addition, labeled antibody when used in the sandwich format), the resulting negatively charged complex is captured with a positively charged solid phase (col. 6, lines 60-65) and removed from the reaction mixture (col. 18, line 64, to col. 19, line 4), where it is then detected (col. 19, lines 8-12). The thrust of Kline's invention is to provide a solution-phase analog to an enzyme-linked immunosorbent assay (ELISA) in order to avoid the difficulties of carrying out protein binding reactions near surfaces (col. 7, lines 4-11; also note that all detection in the examples is carried out enzymatically (alkaline phosphatase operating on a fluorogenic substrate)). In Kline, a charged capture reagent is combined with an oppositely charged solid phase to remove binding compound-analyte complexes from a reaction mixture for detection, whereas in Applicants' invention, charged capture agents are combined with unreacted electrophoretic probes and cleavage products thereof to give them a charge opposite of that of released eTag reporters so that they are not electrophoretically separated together. *That is, in Kline, a moiety is captured so that it can be detected, whereas, in Applicants' invention, a moiety is captured to prevent it from being detected.* Applicants' use of such charged capture agents results in a dramatic increase in resolution of electrophoretically separated eTag reporters, as illustrated in Figs. 26 and 27 of the application. Applicants submit that neither Kline nor Grossman, either alone or together, disclose or suggest, or provide motivation of, the concept of using charged capture agents to bind to *undesired* components of a reaction mixture to exclude them from being separated and detected

with oppositely charged reporter molecules, thereby increasing the sensitivity of assay measurements.

In view of the above, Applicants submit that the cited references have been inappropriately combined and do not render Applicants' invention obvious to one of ordinary skill in the art. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In paragraph 6 of the Office Action, the Examiner rejected claim 22 under 35 U.S.C. 103(a) as being unpatentable over Grossman (cited above) in view of Kline (cited above) as applied above, and further in view of Huie (5,470,967). The Examiner applied Grossman and Kline as described above, and further cited Huie for its disclosure of nuclease-resistant inter-nucleoside linkages.

Applicants respectfully disagree with this rejection for the reasons given above regarding the application of Grossman and Kline, and for the reasons given on pages 9-10 of the Second Amendment dated 21 February 2003. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In paragraph 7 of the Office Action, the Examiner rejected claim 29 under 35 U.S.C. 103(a) as being unpatentable over Grossman (cited above) in view of Kline (cited above) and further in view of Ullman (U.S. patent 6,251,581). The Examiner applied Grossman and Kline as above and further argued that the specific structures recited in claim 29 are disclosed by the chemiluminescent compounds of Ullman.

Applicants respectfully disagree. First, as stated above, Applicants submit that Grossman and Kline have been inappropriately combined. Second, although Ullman discloses compounds similar to those recited in claim 29, the *compositions of Applicants' invention comprise pluralities of such compounds that form distinct peaks in an electropherogram upon electrophoretic separation.* Such compositions are neither disclosed nor suggested by Ullman. In fact, Ullman teaches away from such compositions because his objective is to provide a homogeneous assay based solely on optical (chemiluminescent) detection without any separation of the optically detected molecules; consequently, one of ordinary skill in the art would not be motivated to combine the teaching of Ullman with that of Grossman and Kline. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In view of the above, Applicants submit that the claims as written fully satisfy the requirements of Title 35 of the U.S. Code, and respectfully request that the rejections thereunder be withdrawn and that the claims be allowed and the application quickly passed to issue.

If any additional time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account **50-2266**.

Respectfully submitted,

Stephen C. Macevicz
Reg. No. 30,285
Attorney for Applicants

Telephone: (650) 210-1223
Email: smacevicz@aclara.com

Enclosures:

Petition for Time Extension
Transmittal cover sheet with deposit account withdrawl authorization.